PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

KAW

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

To:
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021216-000610PC

Date of mailing (*day/month/year*) 27 APR 2005

Applicant's or agent's file reference
21216-6-1PC

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/36577	02 November 2004 (02.11.2004)	03 November 2003 (03.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): G01N 33/54, 33/58, 33/52 and US Cl.: 436/537, 800, 805, 808, 826; 252/316; 422/61

Applicant

INTEGRIGEN, INC.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. 7/27/05

For further options, see Form PCT/ISA/220. 9/3/05

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Pensee T. Do Telephone No. 571-272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

Response to Written opinion 9/3/05
DOCKETED BY rfk

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO
Inventive step (IS)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO
Industrial applicability (IA)	Claims Please See Continuation Sheet	YES
	Claims Please See Continuation Sheet	NO

2. Citations and explanations:

Claims 1-4, 6-8, 11-19, 21-23, 26-33, 35-37, 40-51, 54-60, 62-65 lack an inventive step under PCT Article 33(3) as being obvious over MANDLE et al. (US 4,372,745) in view of TARCHA et al. (US 5,252,459).

MANDLE teaches reagents for used in an assay and a method of detecting an analyte by combining a fluorescer label with a binding member to form a conjugate; contacting such conjugate with an analyte of interest that binds to the binding member to form a complex; separating the unbound label conjugates; adding to the separated complex an oxalate ester to carry out an oxidizing reaction . The fluorescer label is capable of accepting the chemical energy from the oxalate ester. The fluorescer is zinc metalo porphyrins, rhodamine-B200-isothiocyanate which comprises of a parent heteroaromatic ring system, a cyanide dye or a rhodamine dye or a fluorescein dye. The binding pair members are antigen and antibody; complementary nucleic acids, a protein and a nucleic acid. The solid support is a bead or a gel. The method of sequencing a target nucleic acid is inherent because the assay can be performed using nucleic acid as a binding member. The oxalic ester comprises of an electronegative constituent such as chlorine; (see col. 19, lines 42-49; col. 8, line 54-col. 9, line 9; col. 10, lines 51-68; col. 11, lines 27-30).

However, MANDLE fails to teach an assay format wherein the label is attached to a binding member and the other binding member is attached to a solid phase.

TARCHA teaches several assay formats among which is a heterogeneous direct assay. In such format, the label is attached to an antibody/binding member, the other binding member is attached to a solid phase. (see col. 6, lines 20-59).

It would have been obvious to one of ordinary skills in the art to use the direct assay format taught by TARCHA in using the reagents taught by MANDLE because such an assay format suggested by TARCHA is well known in the art. It is simple and requires less reagents and method steps.

Claims 5, 9, 10, 20, 24, 25, 34, 38, 39, 52, 53, 61 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest an electronegative constituent comprising of halogen atoms; a fluorophore comprising of a parent xanthene ring;

Claims 1-65 meet industrial applicability because the subject matter claimed can be made or used in industry.

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Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 5, 9, 10, 20, 24, 25, 34, 38, 39, 52, 53, 61
The opinion as to Novelty was negative (No) with respect to claims 1-4, 6- 8, 11-19, 21-23, 26-33, 35- 37, 40-51, 54-60; 62-65
The opinion as to Inventive Step was positive (Yes)with respect to claims 5, 9, 10, 20, 24, 25, 34, 38, 39, 52, 53, 61
The opinion as to Inventive Step was negative(NO) with respect to claims 1-4, 6-8, 11-19, 21-23, 26-33, 35-37, 40-51, 54-60, 62-65
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-65
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE